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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,430	03/18/2002	Lorena Muggetti		1505

22850 7590 05/20/2003

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EXAMINER	
KHARE, DEVESH	

ART UNIT	PAPER NUMBER
1623	5

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,430	MUGGETTI ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. PCT/EP00/07679 .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 1-24 are currently pending in this application.

IDS

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Minor objections

In claims 2-22, the term "A" before the term "formulation" or "product" in line 1, should be changed to "The".

Appropriate correction is required.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

Claims 7,10,11 and 17-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7,10,11,19 and 20 are directed to a formulation according to claim 1 and claims 17 and 18 are directed to a formulation according to claim 14. Claims 7,10,11 and 17-20 do not confer patentable distinction on the previously claimed

formulation claim therefore claims 7,10,11,19 and 20 are being a substantial duplicate of claim 1 and claims 17 and 18 are being substantial duplicate of claim 14. Claims 7,10,11,19 and 20 fail to further limit invention of claim 1 and claims 17 and 18 fails to further limit invention of claim 14. Use limitations in composition claim still given no weight.

Claims 21 and 22 are being substantial duplicate of claim 13. Claims 21 and 22 fail to further limit the estramustine phosphate in lyophilized form or eatramustine phosphate and sulfoalkyl ether cyclodextrin in lyophilized form, of claim 13.

In claim 4, the term "950 mg/m^2 " is unclear. It is unclear whether the "mg/m^2" is a dosage unit.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 23 and 24 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-22 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Martini et al. (WO 96/09072) in combinations with Stella et al. (U.S. Patent 5,134,127) in view of Yoshida et al. (WO 84/02270).

Claims 1-13, 19 and 20-22 are drawn to a pharmaceutical formulation and product containing estramustine phosphate, a sufoalkyl ether cyclodextrin, human albumin and a parenterally acceptable carrier or diluent. Additional claim limitations include the weight ratio of estramustine to sulfoalkyl ether cyclodextrin is from 1:0.5 to 1:5, a single infusion dosage of the estramustine phosphate at least 1300 mg or 950 mg, sulfoalkyl ether cyclodextrin is a straight or branched C1-C6 sulfoalkyl ether cyclodextrin, and estramustine phosphate is in the form of N-methyl glucamine salt or lyophilized form or estramustine phosphate and sulfoalkyl ether cyclodextrin in lyophilized form.

Claims 14-18 are drawn to a pharmaceutical product containing estramustine phosphate, a sufoalkyl ether cyclodextrin, human albumin, a parenterally acceptable carrier or diluent and one or more chemotherapeutic agents. Additional claim limitations include the sulfoalkyl ether cyclodextrin is sulfoalkyl ether β-cyclodextrin and chemotherapeutic agent is doxorubicin or vinblastine.

Martini et al. teach a composition comprising an estramustine phosphate and a cyclodextrin (see abstract). Martini et al. disclosed the molar ratio between drug (estramustine phosphate) and the cyclodextrin from 1:0.5 to 1:10 (see page 5, lines 17-20) and a pharmaceutical formulation with pharmaceutically acceptable carriers or diluents (see page 6, lines 1-2). Martini et al. also suggest on page 5, lines 4-9, the use of cyclodextrin to permit the passage of the estramustine phosphate in solution and the dosage for oral administration from 50 to 1500 mg (see page 6, lines 4-6). Martini et al. disclosed that the preferred cyclodextrin are β-cyclodextrin (see page 4, line 16). Furthermore, on page 2, lines 1-6, a freeze-dried or lyophilized form of a drug-cyclodextrin complex is suggested. Martini et al. differs from the applicant's invention that Martini et al. do not provide an example of a pharmaceutical composition, comprising the estramustine derivative and a cyclodextrin containing human albumin, however Martini et al. does provide motivation to use estramustine and its disodium salt (page 3, line 15) and a cyclodextrin, for cancer therapy (page 6, lines 9-10). It is noted that Martini et al. does not provide specific disclosures regarding the N-methyl glucamine salt of estramustine phosphate and specifically the cyclodextrin derivative: sulfoalkyl ether cyclodextrin.

Stella et al. teach a method of using sulfoalkyl ether cyclodextrin derivatives as solubilizing agents for water insoluble drugs for oral, intranasal, or parenteral administration (see abstract). Stella et al. disclose a composition on col. 7,line 39, containing the complex of sulfoalkyl ether cyclodextrin and estradiol. Stella et al. disclosed the straight or branched cyclodextrin derivatives

on col. 5, lines 29-39). Stella et al. also disclose a pharmaceutical formulation containing a complex of a drug with cyclodextrin derivative together with a pharmaceutical acceptable carrier and optionally other therapeutic agents (see col. 8, lines 34-39). It is noted that Stella et al. does not provide specific disclosures regarding the use of human albumin in the composition.

Yoshida et al. disclose the use of estramustine phosphate in microfine particles as cancer control agent (see page 1, lines 1-13). Yoshida et al. disclose that the protein such as albumin can be converted to microfine particle as carriers (see page 5, lines 12-13). Yoshida et al. also disclose that other cancer control agents such as doxorubin hydrochloride or vinblastine sulfate can be used along with the microfine particles bound to estramustine phosphate (see page 7, lines 15-19). It is noted that Yoshida et al. do not disclose the use of the cyclodextrin in the composition.

Therefore, one of ordinary skill in the art would have found the applicants claimed pharmaceutical formulation and product containing estramustine phosphate, a sufoalkyl ether cyclodextrin, human albumin and a parenterally acceptable carrier or diluent, to have been obvious at the time the invention was made having the above cited references before him. Since Martini et al. teach a composition comprising an estramustine phosphate and a cyclodextrin, Stella et al. teach a method of using sulfoalkyl ether cyclodextrin derivatives as solubilizing agents for water insoluble drug such as estradiol, and Yoshida et al. disclose the use of estramustine phosphate in microfine particles where albumin can be converted to microfine particle as carriers, one skilled in the art would have a reasonable

expectation for success in combining the teachings of these references to accomplish a pharmaceutical formulation or a product containing estramustine phosphate, a sufoalkyl ether cyclodextrin, human albumin and a parenterally acceptable carrier or diluent . The motivation for doing so is provided by Martini et al., which disclose a pharmaceutical composition containing the estramustine derivative and a cyclodextrin, suitable for oral administration of estramustine derivative to a cancer patient.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is (703)605-

1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Devesh Khare, Ph.D.,JD(3Y).
Art Unit 1623
May 19,2003